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Continuation of Application No.: 10/149,549

## **IN THE CLAIMS:**

formula

Claim 1 (currently amended and reformatted): A compound of general

$$R^2$$
 $R^3$ 
 $R^1$ 
 $R^3$ 
 $R^3$ 

wherein D represents CH<sub>2</sub> or CH<sub>2</sub>CH<sub>2</sub>;

E represents C(O)NH or NHC(O);

 $R^1$  and  $R^2$  each independently represent hydrogen, halogen, amino, nitro,  $C_1\text{-}C_6$  alkyl or trifluoromethyl, but R<sup>1</sup> and R<sup>2</sup> may not both simultaneously represent hydrogen; R<sup>3</sup> represents a group of formula

$$R^4\chi$$
  $R^5$  (II);

R<sup>4</sup> represents a C<sub>1</sub>-C<sub>6</sub> alkyl group;

X represents an oxygen or sulphur atom or a group NR 13, SO or SO2;

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R<sup>5</sup> represents hydrogen, or R<sup>5</sup> represents C<sub>1</sub>-C<sub>6</sub>-alkyl or C<sub>2</sub>-C<sub>6</sub> alkenyl, each of which may be optionally substituted by at least one substituent selected from halogen, hydroxyl, (di)-C<sub>1</sub>-C<sub>6</sub>-alkylamino, -Y-R<sup>6</sup>,

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a 5 or 6-membered heteroaromatic ring comprising from 1 to 4 heteroatoms independently selected from nitrogen, oxygen and sulphur which heteroaromatic ring may itself be optionally substituted by at least one substituent selected from halogen, hydroxyl and  $C_1$ - $C_6$ -alkyl;

Y represents an oxygen or sulphur atom or a group NH, SO or SO2;

 $R^6$  represents a group  $-R^7$ Z where  $R^7$  represents a  $C_2$ - $C_6$  alkyl group and Z represents an -OH,  $-CO_2H$ ,  $-NR^8R^9$ ,  $-C(O)NR^{10}R^{11}$  or  $-N(R^{12})C(O)$ - $C_1$ - $C_6$  alkyl group, and, in the case where Y represents an oxygen or sulphur atom or a group NH,  $R^6$  additionally represents hydrogen,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkylcarbonyl,  $C_1$ - $C_6$  alkoxycarbonyl,  $C(O)NR^{14}R^{15}$ ,  $-CH_2OC(O)R^{16}$ ,  $-CH_2OC(O)OR^{17}$ -or  $-C(O)OCH_2OR^{18}$ ;

R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> each independently represent a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub>-alkyl group;

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 $R^{13}$  represents hydrogen,  $C_3$ - $C_8$  cycloalkyl,  $C_3$ - $C_8$  cycloalkylmethyl, or  $R^{13}$  represents a  $C_1$ - $C_6$  alkyl group optionally substituted by at least one substituent selected from hydroxyl and  $C_1$ - $C_6$  alkoxy; and

 $R^{14}$ ,  $R^{15}$ ,  $R^{16}$ ,  $R^{17}$  and  $R^{18}$  each independently represent a  $C_1$ - $C_6$  alkyl group; with the proviso that when E is C(O)NH, X is <u>not-O</u>, NH or N(C<sub>1</sub>-C<sub>6</sub> alkyl), then  $R^5$  is other than a hydrogen atom or an unsubstituted  $C_1$ - $C_6$  alkyl group; or a pharmaceutically acceptable salt or solvate thereof.

Claim 2 (original): A compound according to claim 1, wherein D represents CH<sub>2</sub>.

Claim 3 (currently amended): A compound according to claim 1-or claim 2, wherein E represents NHC(O).

Claim 4 (currently amended): A compound according to any one of claims 1 to 3 claim 1, wherein  $R^1$  and  $R^2$  each independently represent a hydrogen, chlorine or bromine atom, or an amino, nitro,  $C_1$ - $C_3$  alkyl or trifluoromethyl group.

Claim 5 (cancelled).

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Claim 6 (currently amended): A compound according to claim  $\underline{1-5}$ , wherein  $\underline{X}$ represents a group NR<sup>13</sup> in which R<sup>13</sup> represents hydrogen, -(CH<sub>2</sub>)<sub>2</sub>OH, methyl, ethyl, npropyl, isopropyl, n-butyl, n-pentyl, n-hexyl, cyclopropyl, cyclopentyl, cyclohexyl or cyclohexylmethyl.

Claims 7-9 (cancelled).

Claim 10 (currently amended and reformatted): A compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, according to claim 1 which is selected from:

- 2-Chloro-5-[[2-(2-hydroxy-ethylamino]-methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide dihydrochloride,
- 2-Chloro-5-[[2-(2-hydroxyethoxy)ethylamino]methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1ylmethyl)-benzamide,
- 2-Chloro-5-[(3-hydroxy-2,2-dimethylpropylamino)methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1ylmethyl)-benzamide,
- 2-Chloro-5-[(5-hydroxypentylamino)methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[[2-[(2-hydroxyethylthio)ethylamino]methyl]-N (tricyclo[3.3.1.1<sup>3,7</sup>]dec-1ylmethyl) benzamide,
- 2-Chloro-5-[3-[(2-hydroxyethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide, acetate salt,

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2-Chloro-5-[3-[(3-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-vlmethyl)benzamide, hydrochloride salt,

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- 2-Chloro-5-[3-(methylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide, acetate salt.
- 2-Chloro-5-[3-[(1-methylethyl)amino]propyl]-N-(tricyclo[3,3,1,1<sup>3,7</sup>]dec-1-ylmethyl)benzamide, hydrochloride salt,
- 5-[3-[(2-Amino-2-methylpropyl)amino]propyl]-2-chloro-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1ylmethyl) benzamide, dihyrdrochloride salt,
- 2-Chloro-5-[3-[(4-hydroxybutyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-[(2-hydroxy-2-methylpropyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1ylmethyl)-benzamide, acetate salt,
- 2-Chloro-5-[3-[[2-(methylamino)ethyl]amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1ylmethyl)-benzamide, dihydrochloride salt,
- (S)-2-Chloro-5-[3-[(2-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1ylmethyl)-benzamide, hydrochloride salt,
- (R)-2-Chloro-5-[3-[(2-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1ylmethyl)-benzamide, hydrochloride salt,
- (R)-2-Chloro-5-[3-[(2-hydroxy-1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 2-Chloro-5-[3-[[2-hydroxy-1-(hydroxymethyl)-1-methylethyl]amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

5-[3-[[2 (Acetylamino)ethyl]amino]propyl]-2-chloro-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl) benzamide, hydrochloride salt.

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- 2-Chloro-5-[3-[[2-(diethylamino)ethyl]amino]propyl] N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide, dihydrochloride salt,
- 2-Chloro-5-[3-[(3-methoxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 2-Chloro-5-[3-[(3-hydroxy-3-methylbutyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 2-Chloro-5-[3-[(2-methoxyethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide, hydrochloride salt,
- 2-Chloro-5-[[3-(methylamino)propoxy]methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl) benzamide.
- 2-Chloro-5-[[2-[(2-hydroxyethyl)amino]ethoxy]methyl] N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide, acetic acid salt,
- 2-Chloro-5-[[2-[(3-hydroxypropyl)amino]ethoxy]methyl]-N (tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl) benzamide, acetic acid salt,
- 2-Chloro-5-[[[3-[(1-methylethyl)amino]propyl]amino]methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl) benzamide,
- 5-[[(3-Aminopropyl)amino]methyl]-2-chloro-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[[[2-[(1-methylethyl)amino]ethyl]amino]methyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,



3-[[3-[4-Chloro-3-[[(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)amino]carbonyl]phenyl]propyl]amino]propanoic acid, 2,2 dimethylpropyl ester,
trifluoroacetic acid salt,

- 5-(2-Aminoethyl)-2-chloro-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-[(2-hydroxyethyl)pentylamino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(methyl-2-propenylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide.
- 2-Chloro-5-[3-[[2 (dimethylamino)ethyl]methylamino]propyl] N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide.
- 5-[3-(Butylethylamino)propyl] 2-chloro N (tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(methylpentylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5 [3-[[2-(diethylamino)ethyl]ethylamino]propyl] N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(2-hydroxyethyl)methylamino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl) benzamide,
- 2-Chloro-5-[3-(dipropylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>|dec-1-ylmethyl)-benzamide,
- 2-Chloro-5 [3-[(2-hydroxyethyl)(1-methylethyl)amino]propyl] N (tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl) benzamide,
- 5-[3-[Butyl(2-hydroxyethyl)amino]propyl]-2-chloro-N (tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl) benzamide;

- 2-Chloro-5-[3-(diethylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(dimethylamino)propyl]-N (tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 5-[3-(Butylmethylamino)propyl]-2-chloro-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide.
- 2-Chloro-5-[3-[(2-hydroxyethyl)propylamino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide.
- 2 Chloro-5-[3-[ethyl(2-hydroxyethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(dibutylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(ethylpropylamino)propyl] N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide.
- 2-Chloro-5-[3-[methyl(1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[3 (dimethylamino)propyl]methylamino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[eyelohexyl(2-hydroxyethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(cyclohexylmethylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide.
- 2-Chloro-5-[3-(cyclohexylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[1-(hydroxymethyl)-2,2-dimethylpropyl]amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

- 2-Chloro-5-[3-(cyclopropylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[2-(dimethylamino)ethyl]amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec 1-ylmethyl) benzamide,
- 2-Chloro-5-[3-[(3-hydroxy-2,2-dimethylpropyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(1,1-dimethylethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[3-(dimethylamino)propyl]amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-(cyclopentylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-5-[3-[(1,2,2-trimethylpropyl)amino]propyl]-benzamide,
- 5-[3-(Butylamino)propyl]-2-chloro-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[1-(hydroxymethyl)-2-methylpropyl]amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(1-methylpropyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[2-(methylthio)ethyl]amino]propyl] N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(2-hydroxy-1,1-dimethylethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,

- 2-Chloro-5-[3-[(cyclohexylmethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide, and
- 2-Chloro-5-[3-(2-propenylamino)propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(2-fluoroethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[(2-methoxy-1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide.
- 2-Chloro-5-[3-[3-(methylamino)propoxy]propyl]-N (tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide, dihydrochloride salt,
- 5-[[[(1-Aminocyclopropyl)methyl](2-hydroxyethyl)amino]methyl]-2-chloro-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec 1-ylmethyl) benzamide,
- 5-[[(2-Hydroxyethyl)[2 (methylamino)ethyl]amino]methyl]-2-methyl-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)-benzamide,
- 2-Chloro-5-[3-[[2-(1-methyl-1H-imidazol-4-yl)ethyl]amino]propyl] N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide,
- 2-Chloro-5-[3-[[2-(1H-imidazol-4-yl)ethyl]amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide, and
- 2-Chloro-5-[3-[[3-(1H-imidazol-1-yl)propyl]amino]propyl]-N-(tricyclo[3.3.1.1<sup>3,7</sup>]dec-1-ylmethyl)benzamide.

Claim 11 (currently amended and reformatted): A process for the preparation of a compound of formula (I) as defined in claim 1 which comprises:

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(a) when X represents an oxygen or sulphur atom or a group NR <sup>13</sup>, reacting a compound of general formula

$$R^2$$
 $R^4$ - $L^1$ 
 $R^1$ 
(III)

wherein  $L^1$  represents a leaving group and D, E,  $R^1$ ,  $R^2$  and  $R^4$  are as defined in formula (I), with a compound of general formula

wherein R<sup>5</sup> and R<sup>13</sup> are X' represents an oxygen or sulphur atom or a group NR<sup>13</sup>, and R<sup>5</sup> is as defined in formula (I), optionally in the presence of a suitable silver salt; or

(b) when X represents SO or SO<sub>2</sub>, reacting a corresponding compound of formula (I) in which X represents a sulphur atom with a suitable oxidising agent; or

(b)(c) when X represents a group NR<sup>13</sup>, reacting a compound of general formula

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wherein  $R^{20}$  represents a bond or  $C_1$ - $C_5$  alkyl group and D, E,  $R^1$  and  $R^2$  are as defined in formula (I), with a compound of general formula (VI) as defined in (a) above

$$\frac{H_{N}R^{5}}{R^{13}}$$
(VI);

wherein R<sup>5</sup> and R<sup>13</sup> are as defined in formula (I), in the presence of a reducing agent; and optionally after (a), or (b) or (c) converting the compound of formula (I) obtained to a pharmaceutically acceptable salt or solvate thereof.

Claim 12 (currently amended): A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed

in any one of claims 1-4, 6 and 10 1 to 10 in association with a pharmaceutically acceptable

adjuvant, diluent or carrier.

Claim 13 (currently amended): A process for the preparation of a pharmaceutical

composition as claimed in claim 12 which comprises mixing a compound of formula (I), or a

pharmaceutically acceptable salt or solvate thereof, as defined in any one of claims 1-4, 6 and

<u>10-1-to-10</u> with a pharmaceutically acceptable adjuvant, diluent or carrier.

Claims 14-19 (cancelled).

Claim 20 (currently amended): A method of effecting immunosuppression which

comprises administering a therapeutically effective amount of a compound of formula (I), or

a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1-4, 6

and 10-1 to 10 to a patient in need thereof.

Claim 21 (currently amended): A method of treating rheumatoid arthritis which

comprises administering a therapeutically effective amount of a compound of formula (I), or

a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1-4, 6

and 10-1 to 10 to a patient in need thereof.

Claim 22 (currently amended): A method of treating chronic obstructive pulmonary

disease which comprises administering a therapeutically effective amount of a compound of

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formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1-4, 6 and 10-1 to 10 to a patient in need thereof.